REMARKS

Claims 5, 7-27 and 33-34 and 36-37 are pending. Claims 8-9, 12, 14-17, 20-22 and 24-27 are withdrawn. Claims 1-4, 6, 28-32, 35 and 38-41 are canceled without prejudice. Claims 5 and 33 are amended to recite that the uracil analog is not the corresponding nucleoside and that the phosphoribosyl transferase is exogenous to the cell.

The Applicants note that according to *In re Johnson*[1] an element that is positively recited in the specification may be explicitly excluded in the claims. Because support for "The purine or pyrimidine analog can be provided ..... in the form of the corresponding nucleoside" is found in the specification on page 7, paragraph 23, the Applicants believe that no new matter is added by this amendment. Support for "phosphoribosyl transferase is exogenous to said cell" is found in the specification, for example, page, 6, paragraph 20.

Claims 33-34 have been rejected under 35 U.S.C. 102(b) as being anticipated by Shibata et al. (1982) Plant and Cell Physiol. Vol: 23(3):365-374.

The Applicants respectfully submit that the claimed subject matter is not anticipated by the cited reference. Independent claim 33 recites, *inter alia*, biosynthetically labeling RNA in a cell of interest by contacting the cell with a uracil analog having a reactive thiol moiety not normally present in RNA, wherein said cell comprises a uracil phosphoribosyltransferase (UPRT) and wherein said uracil analog is not the corresponding nucleoside and said UPRT is exogenous to the cell.

The Office Action asserts that Shibata teaches contacting radish seedlings with a [2-^{14}C]-4-thiouracil, wherein the cell comprises UPRT (Shibata, Abstract) and the 4-thiouracil is incorporated into RNA synthesized by the cell (Shibata, page 368, ¶1).

The Applicants respectfully submit the rejected claims require that the UPRT be exogenous to the cell. Shibata fails to disclose that the UPRT is exogenous to the radish seedling. Accordingly, Shibata cannot anticipate the rejected claims.

In view of the above, the Applicants respectfully request the withdrawal of the §102(b) rejection of claims 33-34.

Claims 5, 7, 10-11, 13, 18-19 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Melvin et al. (1978) Eur. J. Biochem. 92:373-379 and as evidenced by

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[1] *In re Johnson* 558 F.2d 1008, 1019, 194 USPQ 187, 196 (CCPA 1977)

Woodward et al. (1998) Analytical biochemistry 171:166-172 (both references provided by applicant in IDS) in view of Rana (P.G. Pub 2004/0175732 filed on November 17, 2003 with a priority date of November 15, 2002) as evidenced by Diamandis and Christopoulos (1991) Clin Chem 37 (5) pp 625-636 (provided by Applicant in IDS).

Independent claim 5 recites *inter alia*, biosynthetically labeling RNA in a cell of interest by contacting the cell with a uracil analog having a reactive thiol moiety not normally present in RNA, wherein said cell comprises a phosphoribosyltransferase (UPRT) and wherein said uracil analog is not the corresponding nucleoside and said UPRT is exogenous to the cell.

The Office Action states that Melvin teaches contacting Hamster kidney cell line with 4-thiouridine (4-TU), wherein the cell contains either phosphoribosyl transferase or nucleoside kinase (as evidenced by the labeling of RNA with thiol moiety) and obtaining labeled RNA. (Office Action, dated June 6, 2008, page 7).

The Applicants respectfully submit that 4-thiouridine and uracil are not equivalent compounds chemically or biologically and that claim 5 specifically recites that the uracil analog is not the corresponding nucleoside. Since, Melvin teaches using 4- thiouridine, a nucleoside, Melvin fails to render claim 5 and its dependents obvious.

Moreover, the rejected claims require that the cells comprise a phosphoribosyl transferase. The Office Action states that the Applicants correctly argued that mammalian cells do not have phosphoribosyl transferase. (Office Action, dated June 6, 2008, page 4). Accordingly, Melvin fails to teach or suggest that the Hamster kidney cell "comprises a phosphoribosyl transferase".

Regarding claim 5, Rana is cited for its teachings of incorporating a thiol moiety into miRNA and using biotin as a small molecule binding partner. Diamandis and Christopoulos are cited for teaching a method for biotinylating 4-thiouridine containing nucleic acid. No teaching from Woodward is cited. None of these references teach or suggest, *inter alia*, contacting a cell with a uracil analog where the uracil analog is not the corresponding nucleoside and that the cell comprises a phosphoribosyl transferase as required by claim 5 and its dependents. Accordingly, the combination of Melvin, Woodward, Rana and Diamandis and Christopoulos fails to render claim 5 and its dependents obvious.

In view of the above, the §103 (a) rejection of claims 5, 7, 10-11, 13, 18-19 may be withdrawn.

Claim 35 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shibata et al. as applied to claims 33 and 34 above further in view of Al-Anouti et al. (January 2003) Biochemical and Biophysical Research Communications vol. 302: pp. 316-323—Previously provided to applicant).

Claim 35 is canceled rendering this rejection moot. The element of claim 35 is incorporated into claim 33, accordingly, claim 33 requires that the cell comprises a UPRT that can convert a uracil analog to the corresponding uridine monophosphate and that the UPRT is exogenous to the cell.

The Office Action states that Al-Anouti teaches a pUC19 UPRT plasmid that can be propagated in *E. coli*, thus Al-Anouti teaches that UPRT gene from *T. gondii* is exogenous to the cell.

Al-Anouti discusses using pUC19 UPRT plasmid for deleting an 80 nt internal fragment (Al-Anouti, Materials and methods, section titled Plasmids) and using the resulting plasmid for *in vitro* generation of sense and antisense RNA to generate double stranded RNA (Al-Anouti, Materials and methods, section titled Oligonucleotides; and Transient down-regulation by the dsRNA). However, Al-Anouti does not teach or suggest a cell comprising a UPRT that can convert a uracil analog to the corresponding uridine monophosphate.

Al-Anouti is directed to a method of modulating gene expression of *T. gondii* using dsRNA produced either *in vitro* or *in vivo*. In accordance with the methods disclosed by Al-Anouti, a *T. gondii* parasite is transfected either with a vector containing the genetic sequence for UPRT, from which dsRNA homologous to UPRT is produced or with dsRNA produced *in vitro* (Al-Anouti abstract). The dsRNA is processed into small interfering RNA (siRNA) which then triggers the degradation of the *T. gondii* UPRT mRNA, resulting in decreased UPRT activity. See page 323, 2nd full paragraph. Thus, Al-Anouti proposes a method for decreasing UPRT activity, not for utilizing UPRT activity in the biosynthetic labeling of RNA.

The assertion that the authors designed a plasmid to express UPRT in bacteria and human foreskin fibroblast (HFFs) is not correct. The growth in bacteria is simply for generating plasmid DNA and the construct is never put into HFF cells, the HFF cells are hosts for Toxoplasma that are transfected with the plasmid. There is no transgenic expression of UPRT in an organism other than Toxoplasma in this paper.

The Applicants do not dispute that a wide variety of phosphoribosyltransferases have been cloned and expressed from a wide variety of vectors. However, it is the specific use of the

enzymes in Applicants' methods that is claimed, and the sum of the references does not provide essential features of the present invention.

Moreover, one of skill in the art would have no motivation to modify the radish seedlings of Shibata to express an exogenous UPRT because the radish seedlings have an endogenous UPRT.

In view of the above remarks, withdrawal of the rejection is requested.

Claim 36 is rejected under 35 U.S.C. 103(a) as being unpatentable over Shibata as applied to claims 33 above further in view of Maddry (US Pat. 5,561,225, Oct. 1, 1996) as evidenced by Chan (US Pat. 6,403,311 B1 filed Aug. 13, 1999) and evidenced by Diamandis and Christopoulos (1991) Clin Chem 37 (5) pp 625-636 (provided by Applicant in IDS).

The Applicants respectfully submit that Shibata does not teach or suggest the presently claimed invention, as discussed above.

Maddry teaches that 2, 4-dithiouracil is a uracil analog; a fact that is not disputed by the Applicants, although in combination with the primary reference, it does not teach or suggest the presently claimed invention.

Applicants respectfully submit that the present claims meet the requirements of 35 U.S.C. 103(a). Withdrawal of the rejection is requested.

CONCLUSION

Applicant submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number STAN-304.

Respectfully submitted,
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Date: September 8, 2008

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